Executive Summary

CDMRP Vision: To find and fund the best research to eradicate diseases and support the warfighter for the benefit of the American public.

CDMRP Mission: To provide hope by promoting innovative research, recognizing untapped opportunities, creating partnerships, and guarding the public trust.

"The time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease. Let us make a total national commitment to achieve this goal."

—President Richard M. Nixon, referring to cancer in his State of the Union Speech, January 22, 1971

Introduction

In 1971, the "War on Cancer" began when President Richard M. Nixon challenged the nation to find a cure for cancer. Today, billions of dollars are spent every year to meet this challenge. This investment has produced an explosion in biomedical research that has begun to have a substantial impact in the clinic. Scientific knowledge has grown exponentially in the past three decades due to the efforts of researchers, physicians, cancer advocates, and funding organizations. A key player in this endeavor is the Office of the Congressionally Directed Medical Research Programs (CDMRP).

The CDMRP, a division of the U.S. Army Medical Research and Materiel Command (USAMRMC), is located at Fort Detrick in Frederick, Maryland. Although the USAMRMC normally focuses on research and technology appropriate to national defense, the CDMRP has been mandated by Congress to seek out, identify, and fund research targeted at curing and eradicating cancer and other diseases. To prevent an overlap of effort with other funding organizations, the CDMRP has instituted several significant changes in the grant management process, not the least of which is the involvement of people who have survived disease (i.e., "consumers") in all phases of the funding process.

Program History

The USAMRMC's foray into cancer research began in 1992 with the congressional appropriation of $25 million (M) for "Army breast cancer research." Also in 1992, the National Breast Cancer Coalition (NBCC), headed by Ms. Fran Visco, was raising public and legislative awareness of the scarcity of breast cancer funding. The NBCC collected 2.6M signatures (one for each American diagnosed with breast cancer) on a petition asking the government for a comprehensive plan to find a cure for breast cancer. This massive undertaking was presented to President Bill Clinton in 1992, which led Congress to increase the USAMRMC's mandate with an additional $210M in funding for fiscal year 1993 (FY93). This extraordinary level of funding prompted the USAMRMC to create the CDMRP to manage its new Breast Cancer Research Program (BCRP).

Because of the success of the CDMRP, Congress has increased the CDMRP's portfolio to 40 research programs funded by $3.0 billion (B) dollars through FY04. Eight core programs managed by the CDMRP focus on breast, prostate, and ovarian cancers; neurofibromatosis; military health; chronic myelogenous leukemia; tuberous sclerosis complex; and myeloproliferative diseases.

Program Development, Execution, and Evaluation

The Army has a need for research, development, logistics, and acquisition activities targeted at medical problems emphasized by life in the military. The USAMRMC, which manages these needs, operates six medical research laboratories and institutes in the United States and worldwide that are centers of excellence in specific areas of biomedical research. Cooperative agreements with

leading civilian organizations and funding of extramural research complement and enhance the Army's intramural programs. Despite the wide breadth and excellent quality of the USAMRMC's research, breast cancer was outside the Army's expertise. Therefore, the USAMRMC solicited advice from the National Academy of Sciences Institute of Medicine (IOM) on how to identify gaps in breast cancer research and how this new appropriation could best be used. This collaboration resulted in two important implementations in the CDMRP management style.

First, a council of experts in breast cancer advocacy, research, and clinical practice was formed to produce a vision of the research strategy that would address the current needs of breast cancer research. Similar councils, or Integration Panels (IPs), are now convened for each of the core programs currently managed by the CDMRP. The vision of each program is updated annually so that the program's focus is adjusted to the current research environment. Secondly, the IOM advised that the CDMRP institute a two-tier review process: the first tier to assess the scientific merit of proposals and the second to decide funding based on the vision set by the IP. This allows the CDMRP to fund excellent, timely research that meets the ever-changing demands of the research communities.

Another strength of the CDMRP is the management of awards after funding. A certain level of unpredictability is intrinsic to research – particularly with novel research. Because the CDMRP's focus is on novel research, this unpredictability raises the likelihood that funded research will stray from the program's intention. To ensure that these projects remain true to the vision of the program, progress is closely monitored. In addition, the CDMRP is constantly monitoring and evaluating its own portfolio to make certain its congressional mandate is being met.

Part of the CDMRP's mandate is to make sure that its appropriations are wisely spent – not only scientifically, but also managerially. The CDMRP noticed that the current manner of submitting, distributing, and reviewing grants was highly inefficient. For instance, in 1996, the National Institutes of Health recycled 340 tons of paper related to the submission of biomedical grants and every one of these proposals must be physically handled many times.[1] To reduce this waste in materials and man-hours, the CDMRP has become a leader in electronic collection of proposals and dissemination of funding information. Principal Investigators simply need to upload their proposals to the CDMRP website (http://cdmrp.army.mil), which are then distributed electronically to reviewers. The website also contains a plethora of resources and information; for example, program announcements of funding opportunities, research highlights, and annual reports. In addition, the majority of the review process is handled electronically and is expected to become completely paperless in the months following preparation of this report.

Breast Cancer

One out of eight women will develop breast cancer. In 2003, the American Cancer Society estimated that over 200,000[a] new cases of breast cancer were diagnosed in the United States. Although ~90% of these patients will survive more than 5 years, more than 40,000 women were expected to die from the disease in 2003.

In FY04, the BCRP was appropriated $150M bringing the total to $1.7B through FY04 to fight breast cancer. More than 4,000 grants have been awarded.

[a] American Cancer Society-*Cancer Facts and Figures,* 2004

Prostate Cancer

If one discounts the cases of lung cancer due to smoking, prostate cancer is the leading cause of cancer deaths in U.S. males,[a] with approximately 230,000 new cases and 30,000 deaths expected in 2003.

The PCRP was formed in FY97 and since that time $565M has been appropriated for prostate cancer research; $85M in FY04. More than 1,000 grants have been awarded.

[a] American Cancer Society-*Cancer Facts and Figures,* 2004

[1] *The NIH Record*, January 28, 1997.

"Only those who will risk going too far can possibly find out how far one can go".
- T.S. Eliot

Neurofibromatosis

Neurofibromatosis (NF) is a cumulative degenerative proliferative disorder of the nervous system. Two genetic disorders, NF1 and NF2, actually comprise NF. The more common NF1 affects 1 out of every 4,000 people in their lifetime, whereas NF2 affects 1 in 40,000.[a]

In 1996, Congress directed the CDMRP to study NF. Since then, the CDMRP has managed over $130M targeted toward curing this disease. In FY04, $20M of this money was appropriated, making the NFRP the largest publicly funded research program for NF.[b] This burst of funding has greatly advanced our understanding of and ability to treat this disease.

[a] *Report on Neurofibromatosis*, Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Neurological Disorders and Stroke, 2003.

[b] The National Neurofibromatosis Foundation, Inc.

Ovarian Cancer

Approximately 25,500 women were diagnosed with ovarian cancer in 2003. Although ovarian cancer is more than 8-fold less prevalent than breast cancer, patients stand a 2.5-fold greater risk of dying from the disease.[a] Approximately 16,000 women died from ovarian cancer in 2003.

From its inception in 1997, the OCRP has managed $81.7M in appropriations. In FY03, 17 awards were made with the $10M appropriation. An additional $10M was appropriated in FY04.

[a] American Cancer Society-*Cancer Facts and Figures,* 2004

The management innovations made by the CDMRP in vision setting, proposal review, and research evaluation have proved extremely successful in finding and filling gaps in current cancer research. A salute to the success of the CDMRP's improvements to the granting process is that these enhancements are being adopted in whole or in part by other granting organizations. The CDMRP has become a timely and efficient sponsor of innovative and progressive cancer research necessary to prevent, control, and eventually cure these dreaded diseases.

The CDMRP in Fiscal Year 2003

The mission of the CDMRP is to provide hope by promoting innovative research, recognizing untapped opportunities, creating partnerships, and guarding the public trust. The success of the CDMRP's management style and funded research combined with the work of cancer advocacy groups have resulted in continued funding of the program since 1993. Since its inception, the CDMRP has funded 5,627 awards from appropriations of $2.6B. The core research programs are as follows:

- Breast Cancer Research Program (BCRP)
- Prostate Cancer Research Program (PCRP)
- Neurofibromatosis Research Program (NFRP)
- Ovarian Cancer Research Program (OCRP)
- Peer Reviewed Medical Research Program (PRMRP)
- Chronic Myelogenous Leukemia Research Program (CMLRP)
- Tuberous Sclerosis Complex Research Program (TSCRP)

The Vision for the Fiscal Year 2004 Programs

The CDMRP continues to fulfill a unique niche in biomedical research. In FY04, Congress appropriated $366.5M to continue investing in innovative research aimed at understanding and curing life-threatening diseases. The focus of each program has been adjusted based on the latest breakthroughs and innovations in appropriate fields of research. In particular, many new tailor-made award mechanisms have been added that spotlight attention on the development of new treatments and the training of new researchers and clinicians to carry out this work.

Scientific Outcomes and Advances

In simplest terms, the CDMRP's business is to leverage research through whatever means are at its disposal. As an attentive and caring custodian for the American people's money, the CDMRP has invested in people, science management, ideas, collaborations, and technology in its effort to find cures.

Leveraging People to Cure Disease

A unique component of the CDMRP granting mechanism is its reliance on guidance from people with extremely varied backgrounds: research scientists, clinicians, consumers, and members of advocacy groups. Historically, the public has had little if any direct input steering the course of biomedical research; yet the CDMRP has found the involvement of consumers and advocates to be an invaluable asset to the success of the program. Over 600 consumers have been involved in peer review and IPs; even more have aided in patient recruitment, public education, and advising researchers.

Leveraging Science Management to Cure Disease

From the beginning, the CDMRP has employed an adaptable management strategy. In particular, the CDMRP has been a leader in managing grants electronically, including distribution of materials and submission of proposals. In FY03, the CDMRP took another step to streamline the management of grants by launching the Electronic Grants System (EGS), which allows efficient electronic management of grants from receipt to closing. This latest improvement virtually eliminates the paperwork associated with grants management.

Offering new appropriate funding opportunities is a hallmark of the CDMRP. In FY03, new award mechanisms were created to address deficits in cancer research. Many of these award mechanisms specifically targeted deficiencies in training of health care providers and young researchers. Other new mechanisms were created specifically asking for novel and untested hypotheses that, while being high risk, had the potential for high gain. The new mechanisms will infuse the research community with new ideas and excellent researchers.

Leveraging Ideas to Cure Disease

In keeping with recommendations from the IOM and its mandate to fund the best innovative research, the CDMRP funds high-risk, high-gain research that is generally not considered high priority by other granting agencies. Each of the award mechanisms that promote innovative research has different requirements that focus attention on novel approaches, concepts, or technologies.

Leveraging Collaborations to Cure Disease

The exchange of ideas and information is critical to efficient and effective program operations. Collaborative efforts are seen at all levels of the CDMRP: management, recruitment, funding, and scientific reporting. At the managerial level, the CDMRP has formed international collaborations with other granting organizations to pool resources and facilitate the exchange of ideas and knowledge. Realizing that research also benefits from cooperative interactions, the CDMRP has funded consortia, research centers, and program projects that promote frequent communications among researchers. To facilitate the exchange of research findings, the CDMRP also funds research conferences, notably the biannual Era of Hope breast cancer symposia.

Peer Reviewed Medical Research

Members of our military are exposed to occupational health risks not normally experienced by the public. These hazards include infectious diseases, exposure to toxins, and abnormal physical stresses. The PRMRP aims to improve the health of our military by focusing on needs specific to our troops.

The PRMRP has managed $244.5M from FY99–04; 29 proposals were funded from the $50M FY03 appropriation.

Leveraging Technology for Product Development to Cure Disease

The ultimate objective of cancer research is to cure the disease. To attain this goal, new technological resources in the form of drugs, research tools, and instrumentation and diagnosis aids are imperative assets. The CDMRP is proud to have supported some of the most important and innovative technological advances in recent times. Work from Dr. Margo Haygood has shown that bryostatin, a drug from a marine coral-like animal, sensitizes breast cancer to chemotherapy while simultaneously bolstering the immune system, which is often weakened as a side effect of cancer treatments. Detecting cancer early is very important to survival. Dr. Vinata Lokeshwar made a significant advance in detecting prostate cancer using hyaluronic acid and hyaluronidase, allowing an 85% accurate prediction of prostate cancer re-occurrence. An exciting advancement for treating ovarian cancer has come from Dr. Jianling Gong's laboratory. Dr. Gong has found a way to "kick-start" a patient's own immune systems to specifically target the cancer cells; this work will soon enter Phase 1 clinical trials.

Looking Ahead

Cancer is not a single disease, but many diseases sharing the common trait of uncontrolled cell growth. The other commonality these diseases have is the traumatic effects on patients, their families, and society in general. For the good of the individual and our society, we will succeed. There is unlikely to be any "magic bullet" to treat all types of cancer, but recent research has provided ammunition for finding the right combination of therapies to prolong life and eventually cure the disease. The CDMRP vision for 2005 is already largely in place with new emphases driven by new research. Each day brings us more hope and closer to a cure.

Chronic Myelogenous Leukemia

Chronic Myelogenous Leukemia (CML) is a disease caused by the overgrowth of a specific type of white blood cells (granulocytes). In 2003, approximately 4,500 people will be diagnosed with CML and 2,000 of these individuals will die. The rate of occurrence increases from one in 100,000 at age 50 to one in 10,000 by age 80.[a] The current focus of the CMLRP is on the 20% of CML cases that are resistant to Imatinib, the most effective treatment for CML.

The CMLRP began in FY02 with an appropriation of $5M and continues with appropriations of $4.25M in both FY03 and FY04.

[a] The Lymphoma and Leukemia Organization.

Tuberous Sclerosis Complex

Tuberous Sclerosis Complex (TSC) is a disease where tumorous growths develop in any part of the body. Two thirds of the cases are caused by spontaneous mutations in either the TSC1 or TSC2 gene.

Congress mandated funds to study TSC in FY02. Since that time, TSC Research Program has managed $6M in appropriations; $2M in FY03 when 4 grants were awarded. An additional $3M was appropriated in FY04.

Myeloproliferative Disorders

The Myeloproliferative Disorders Research Program (MPDRP) is the newest in the CDMRP. This collection of diseases is typified by overgrowth of blood or bone marrow cells.

The MPDRP is currently managing $4.25M in FY04 funds and expects 6 grants from this appropriation.